AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please delete the paragraph spanning page 1, line 27 through page 2, line 2 and insert the following therefor:

The classification of MT proteins is based on the arrangement of Cys residues. Cobbett and Goldsbrough (Annu Rev Plant Biol. 53, 159-82, 2002) discriminate four classes: Type 1 to Type 4. Type 2 MTs contain two cysteine rich domains separated by a spacer of approximately 40 amino acids, with the first pair of cysteines present as a Cys-Cys motif in amino acid positions 3 and 4. In addition, the sequences of the N-terminal domain of Type 2 MTs (MSCCGGNCGCS-(SEQ ID NO:8)) are highly conserved.

Please delete the paragraph spanning page 6, line 36 through page 7, line 13 and insert the following therefor:

The term metallothionein includes proteins homologous to the metallothionein as presented in SEQ ID NO 2. Metallothioneins are well known in the art, for a recent overview and classification, see Cobbett and Goldsbrough (2002). Metallothioneins are small proteins with a dumbbell conformation that finds its origin in conserved N-terminal and C-terminal cysteine rich domains which are separated from each other by a region that is variable in length and amino acid composition. Based on the primary structure 4 types of metallothioneins are discriminated, an alignment of various plant metallothioneins is given in Figure 1. The metallothionein of SEQ ID NO 2 comprises a

conserved N-terminal domain typical for type 2 metallothioneins as defined by Cobbett and Goldsbrough (2002), which domain comprises the consensus sequence "MSCCGG(N/S)CGCG(T/S/A)(G/A/S)C(K/Q/S)C" (SEQ ID NO:9), accordingly, preferred homologues to be used in the methods of the present invention are metallothioneins comprising this conserved domain. Additionally and/or alternatively, the metallothionein homologues have metal binding activity which can be measured in a metal saturation test (Scheuhammer et al., Toxicol. Appl Pharmacol. 82, 417-425, 1986) and/or may function as a redox sensor (Fabisiak et al., Methods Enzymol. 353, 268-281 (2002)).

Please delete the paragraph spanning lines 15-29 of page 7, and insert the following therefor:

Methods for the search and identification of metallothionein homologues would be well within the realm of a person skilled in the art. Such methods comprise comparison of the sequences represented by SEQ ID NO 1 or 2, in a computer readable format, with sequences that are available in public databases such as MIPS (URL: mips.gsf.de ~~http://mips.gsf.de/~~), GenBank (URL: ncbi.nlm.nih.gov/Genbank/index.html ~~http://www.ncbi.nlm.nih.gov/Genbank/index.html~~) or EMBL Nucleotide Sequence Database (URL:ebi.ac.uk/embl/index.html ~~http://www.ebi.ac.uk/embl/index.html~~), using algorithms well known in the art for the alignment or comparison of sequences, such as GAP (Needleman and Wunsch, J. Mol. Biol. 48; 443-453 (1970)), BESTFIT (using the local homology algorithm of Smith and Waterman (Advances in Applied Mathematics 2; 482-489 (1981))), BLAST (Altschul,

S.F., Gish, W., Miller, W., Myers, E.W. & Lipman, D.J., J. Mol. Biol. 215:403-410 (1990)), FASTA and TFASTA (W. R. Pearson and D. J. Lipman Proc.Natl.Acad.Sci. USA 85:2444- 2448 (1988)). The software for performing BLAST analysis is publicly available through the National Centre for Biotechnology Information. The abovementioned homologues were identified using blast default parameters (BLOSUM62 matrix, gap opening penalty 11 and gap extension penalty 1) and preferably the full length sequences are used for analysis.

Please delete the paragraph spanning page 7, line 31 through page 8, line 12 and insert the following therefor:

"Homologues" of a metallothionein protein encompass peptides, oligopeptides, polypeptides, proteins and enzymes having amino acid substitutions, deletions and/or insertions relative to the unmodified protein in question and having similar biological and functional activity as the unmodified protein from which they are derived. To produce such homologues, amino acids of the protein may be replaced by other amino acids having similar properties (such as similar hydrophobicity, hydrophilicity, antigenicity, propensity to form or break α-helical structures or β-sheet structures). Conservative substitution tables are well known in the art (see for example Creighton (1984) Proteins. W.H. Freeman and Company). The homologues useful in the method according to the invention have at least 50% sequence identity or similarity (functional identity) to the unmodified protein, alternatively at least 60% sequence identity or similarity to an unmodified protein, alternatively at least 70% sequence identity or similarity to an unmodified protein. Typically, the homologues have at least 80% sequence identity or

similarity to an unmodified protein, preferably at least 85% sequence identity or similarity, further preferably at least 90% sequence identity or similarity to an unmodified protein, most preferably at least 95% sequence identity or similarity to an unmodified protein. Preferred homologues include the proteins comprising the conserved sequence "MSCCGG(N/S)CGCG(T/S/A)(G/A/S)C(K/Q/S)C" (SEQ ID NO:9), such as SEQ ID NO 4 or GenBank accessions CAA71803, AAP94016, CAA71804, NP_195858, AAM62956, AAB61212, CAA65009, CAA92243.

Please delete the paragraph spanning page 8, line 32 through page 9, line 6 and insert the following therefor:

Orthologous genes can be identified by querying one or more gene databases with a query gene of interest, using for example the BLAST program. The highest-ranking subject genes that result from the search are then again subjected to a BLAST analysis, and only those subject genes that match again with the query gene are retained as true orthologous genes. For example, to find a rice orthologue of an *Arabidopsis thaliana* gene, one may perform a BLASTN or TBLASTX analysis on a rice database (such as (but not limited to) the *Oryza sativa* Nipponbare database available at the NCBI (URL: ncbi.nlm.nih.gov ~~http://www.ncbi.nlm.nih.gov~~) or the genomic sequences of rice (cultivars indica or japonica)). In a next step, the obtained rice sequences are used in a reverse BLAST analysis using an *Arabidopsis* database. The results may be further refined when the resulting sequences are analysed with ClustalW and visualised in a neighbour joining tree. The method can be used to identify orthologues from many different species.

Please delete the paragraph spanning page 29, line 34 through page 30, line 2 and insert the following therefor:

Figure 1: Alignment of various plant metallothionein sequences (Cobbett and Goldsbrough, 2002). Conserved cysteines in the N-terminal and C-terminal regions are indicated with an asterisk. Abbreviations: At, *Arabidopsis thaliana*~~*vulgaris*~~, Bn, *Brassica napus*, Os, *Oryza sativa*, Ps *Pisum sativum*, Ms, *Medicago sativa*, Bo, *Brassica oleracea*, Ph, *Petunia hybrida*, Sv, *Silene vulgaris*, Ma, *Musa acuminata*, Ad, *Actinidia deliciosa*, Gh, *Gossipium hirsutum*, Pg, *Picea glauca*, Zm, *Zea mays*, Ta, *Triticum aestivum*. The following sequences are displayed: SEQ ID NO:10 (AtMT1a), SEQ ID NO:11 (AtMT1c), SEQ ID NO:12 (BnMT1), SEQ ID NO:13 (OsMT1a), SEQ ID NO:14 (PsMT1), SEQ ID NO:15 (MsMT1), SEQ ID NO:2 (AtMT2a), SEQ ID NO:16 (BoMT2), SEQ ID NO:17 (AtMT2b), SEQ ID NO: 18 (PhMT2), SEQ ID NO: 19 (SvMT2), SEQ ID NO: 20 (OsMT2) SEQ ID NO:21 (AtMT3), SEQ ID NO:22 (MaMT3), SEQ ID NO:23 (AdMT3) SEQ ID NO:24 (OsMT3), SEQ ID NO:25 (GhMT3), SEQ ID NO:26 (PgMT3), SEQ ID NO:27 (AtMT4a), SEQ ID NO:28 (AtMT4b), SEQ ID NO:29 (PhMT4), SEQ ID NO:30 (ZmMT4), SEQ ID NO:31 (TaMT4), and SEQ ID NO:32 (OsMT4).

Please delete the paragraph on line 20 of page 30, and insert the following new paragraph therefor

~~Figure 4: Sequence listing~~

Please insert the attached Sequence Listing in place of the Sequence Listing filed November 1, 2005.